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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,230	06/26/2003	Yoshitake Yamamoto	D-1205CIP	4227

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EXAMINER	
TURK, NEIL N	
ART UNIT	**PAPER NUMBER**
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,230	YAMAMOTO, YOSHITAKE	
	Examiner	Art Unit	
	Neil Turk	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-8* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Remarks

This Office Action fully acknowledges Applicant's remarks filed on December 11th, 2007. Claims 1 and 5-8 are pending. Claims 2-4 have been cancelled. Claim 8 is newly added.

Priority

The disclosure of the prior-filed application, Application No. 10/015,668, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The 10/015,668 application does not provide adequate support or enablement for the subject matter of claim 6. The 10/015,668 disclosure for spectrometry conditions is drawn to positive and negative ion detection modes and not to molecular ion detection and fragment ion detection modes. Thereby, claim 6 will not receive the filing date of the prior-field application, 10/015,668, filed on 12/17/2001.

Claim Objections

Claim6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 6 recites that the control portion executes the mass spectrum in a molecular ion detection mode and a fragment ion detection mode alternately. This recitation is unclear as claim 1 recites that the control portion sequentially executes the cycle of the mass spectrometry

repeatedly. This is further unclear as the ion detection mode and fragment ion detection mode are not defined as the plurality of spectrometry conditions, as recited in claim 1. Claim 6 thereby does not properly further limit independent claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The structural connections between the parts of the device recited in claim 1 are indefinitely recited and unclear. First, the chromatograph portion is connected to an introduction section for separating components, and then there is a flow path branch portion connected to "an" output of the chromatograph portion for analyzing the components (Examiner asserts this should read, "the separated components"). The claim then recites that the mass spectrum acquisition portion is connected to a "first" output of the flow path branch portion. This structural connection here is unclear in the different outputs. Applicant has not properly and clearly established the connection of the chromatogram portion to the flow path portion, which then leads the "**separated** components" to the mass spectrum acquisition portion. These unclear structural connections are further seen in the other recited elements of the device. Applicant should clear up the different outlets from the flow path branch

portion and properly structurally relate the various elements so that they may be functionally operable by proper relative structural connection, as shown in figure 1.

Claims 1 and 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's recitation to the mass spectrum acquisition portion and the control portion is indefinitely recited and hard to understand. The claim recites that the control portion is connected to the mass spectrum acquisition portion for executing a cycle of the mass spectrum acquisition. This is unclear as the mass spectrum acquisition does not recite nor require any functionalities for receiving mass spec data or to any particular cycle that is undertaken in the mass spectrum acquisition portion. The mass spectrum acquisition portion is only defined as being connected to the first output of the flow path for analyzing the components. Examiner asserts that the mass spectrum acquisition portion is missing elements that would be required for mass spectrum acquisition. Thereby its control relative to a cycle of mass spectrum acquisition is not properly defined and is unclear. Further, the recitation to, "...while changing the plurality of spectrometry conditions" is unclear. Are the spectrometry conditions being constantly changed during a process? Is the spectrometry condition changed after a cycle at one particular condition is completed? Further, the recitation, "...said control portion sequentially executing the cycle of the mass spectrometry repeatedly" is unclear. What does this mean? The combination of the terms "sequentially" and "repeatebly" in their context renders this recitation hard to

understand. As there a recited "plurality of spectrometry conditions" that can be set (thereby, possibly more than two conditions), the term sequentially in combination with repeatedly is unclear as there is no distinct repeated pattern to be carried out over and over. Examiner asserts that Applicant should clean up the recitation so as to recited the controller's function more clearly.

Claims 1 and 5-8 recite the limitation "the mass spectrometry". There is insufficient antecedent basis for this limitation in the claim. In all previous instances, the term "mass spectrum acquisition" has been used. Examiner further notes that the mass spectrum acquisition portion has not been recited with any language to receiving mass spectrums.

Claim 6 recites the limitation "the mass spectrum". There is insufficient antecedent basis for this limitation in the claim.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 recites that the control portion executes the mass spectrum in a molecular ion detection mode and a fragment ion detection mode alternately. This recitation is unclear as claim 1 recites that the control portion sequentially executes the cycle of the mass spectrometry repeatedly. This is further unclear as the ion detection mode and fragment ion detection mode are not defined as the plurality of spectrometry conditions, as recited in claim 1. Claim 6 thereby does not properly further limit independent claim 1.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What is an objective component? Claim 1 does not define such components are obtained, found, designated, or otherwise. Further, how does the control portion detect a peak of an objective component? Claim 1 does not recite anything with regards to peaks. The claim is unclear and indefinitely defined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP06102251A (translated Derwent Abstract Acc. No. 1994-161274), hereafter JP, in view of Stevens (4,762,617).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Stevens teaches a chromatogram system with two detectors and a fraction collector (Fig. 1). Chromatogram data are added or subtracted to scale the data (lines 56-58, col. 4).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by the positive and negative ionization detection in order to scale data in a two-detection scheme chromatograph such as taught by Stevens. It would have been obvious to modify the JP device to include a fraction collector to collect desired fractions as taught by Stevens, under control of the detector signal as was known in the art.

Claims 1, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP in view of Windig (6,329,652).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Windig teaches a method for data handling for an LC-MS system. A summation of particular data is plotted to obtain an enhanced chromatogram (lines 1-19, col. 4).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by the positive and/or negative ionization detection in order to enhance chromatograms such as taught by Windig. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP in view of Watanabe (6,444,979).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Watanabe teaches a method for data handling for a chromatogram-MS system. A summation of particular data is plotted to obtain a chromatogram of all mass vs. time (columns 7 and 8, figs. 4-7a).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by positive and/or negative ionization detection in order to provide a cumulative chromatogram as taught by Watanabe. It would have been

obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP in view of Sacks (5,205,845).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Sacks teaches a method for data handling for a chromatographic system. A summation of particular data of the multiple columns forms a single chromatogram from FID 16, and in this way the chromatographic time dimension can be used more efficiently (lines 9-47, col. 8).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by the positive and/or negative ionization detection in order to provide a single chromatogram and thus allow the chromatogram time dimension to be used more efficiently such as taught by Sacks. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1 and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman et al. (A Novel Precursor Ion Discovery Method on a Hybrid-Quadrupole Orthogonal Acceleration Time-of-Flight (Q-TOF) Mass Spectrometer for Studying Protein Phosphorylation, 2002, American Society for Mass Spectrometry), hereafter Bateman, in view of Stevens.

Bateman discloses a liquid chromatograph mass spectrometer system in which a tandem quadrupole time-of-flight (Q-TOF) mass spectrometer has been programmed such that phosphorylated peptides can automatically be discovered and identified. Bateman discloses that alternate mass spectra, with and without fragmentation, are recorded at high and low collision energy. Bateman discloses that the method of the analysis is both compatible with and dependant on liquid chromatography for separation of complex mixtures. The method also incorporates acquisition of the product ion spectrum from any candidate precursor ions, thereby allowing confirmation of the neutral loss or product ion (abstract). Bateman discloses that the number of product ion spectra to be recorded may be further reduced by first testing to determine whether or not the characteristic product ion or neutral loss is present. Bateman discloses that this is accomplished by operating the quadruple mass filter in the RF-only mode such as to simultaneously transmit a decade in mass into the gas collision cell with higher collision energy, sufficient to induce fragmentation. All ions from the source with m/z values above the low mass cut-off value, 0.78 times the set m/z value, of the RF-only quadrupole are transported through the quadrupole and fragmented in the gas collision cell. The orthogonal TOF mass spectrometer then records the mass spectrum of the

resulting mixture of precursor and fragment ions. Bateman further discloses that it is only necessary to switch to low collision energy to prevent fragmentation and hence to record the mass spectrum of precursor ions only. Bateman discloses that by alternating the collision energy, it is possible to alternate between recording the spectrum exhibiting the mixture of precursor ions and their fragment ions. The operating conditions are set such that alternated spectra are recorded under at least two distinct operating modes, such as one of low collision energy (no significant fragmentation), and a second mode of high collision energy (mostly all precursor ions fragmented) (page 794). Bateman discloses that if the two operating modes are suitably set, precursor and product ions may be readily distinguished (page 795, full document).

Bateman does not disclose an operation device for adding data.

Stevens teaches a chromatogram system with two detectors and a fraction collector (Fig. 1). Chromatogram data are added or subtracted to scale the data (lines 56-58, col. 4).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by the fragmented and unfragmented ionization detection in order to scale data in a two-detection scheme chromatograph such as taught by Stevens. It would have been obvious to modify the JP device to include a fraction collector to collect desired fractions as taught by Stevens, under control of the detector signal as was known in the art.

Claims 1 and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman in view of Windig.

Bateman has been discussed above.

Bateman does not disclose an operation device for adding data.

Windig teaches a method for data handling for an LC-MS system. A summation of particular data is plotted to obtain an enhanced chromatogram (lines 1-19, col. 4).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by the fragmented and unfragmented ionization detection in order to enhance chromatograms such as taught by Windig. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1 and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman in view of Watanabe.

Bateman has been discussed above.

Bateman does not disclose an operation device for adding data.

Watanabe teaches a method for data handling for a chromatogram-MS system. A summation of particular data is plotted to obtain a chromatogram of all mass vs. time (columns 7 and 8, figs. 4-7a).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by fragmented and unfragmented detection in order to provide a cumulative chromatogram as taught by Watanabe. It would have been

obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1 and 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman in view of Sacks.

Bateman has been discussed above.

Bateman does not disclose an operation device for adding data.

Sacks teaches a method for data handling for a chromatographic system. A summation of particular data of the multiple columns forms a single chromatogram from FID 16, and in this way the chromatographic time dimension can be used more efficiently (lines 9-47, col. 8).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by the fragmented and unfragmented detection in order to provide a single chromatogram and thus allow the chromatogram time dimension to be used more efficiently such as taught by Sacks. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Response to Arguments

Applicant's arguments filed December 11th, 2007 have been fully considered but they are not persuasive.

With regard to claims 1, 3-5, and 7 rejected under 35 USC 103(a) over JP06102251A (translated Derwent Abstract Acc. No. 1994-161274), hereafter JP, in view of Stevens (4,762,617), Applicant argues that the combination is improper.

Applicant argues that Steven's does not expressly or implicitly indicate that spectrum intensities obtained in the plurality of spectrometry conditions are added for obtaining chromatogram data. Applicant further asserts that it is not disclosed in Stevens that the chromatograms obtained in the two monitors are added, and that the components are collected based on the added chromatograms. Examiner asserts that such arguments are drawn to functional limitations and process limitations. As the claims are currently drawn to an apparatus, such functional and process limitations are not afforded patentable weight. The prior art combination of JP and Stevens recites all of the structure of the claims, and as such, the device is said to be capable of the recited functions. If Applicant wants patentable weight attributed to the function of the specific collection of components in the fraction collector as purported, Applicant must recite control means, software, or other processing element, which detail such functions. As currently recited, Applicant's control means does not relate to and does not recite necessary functions to this selective collecting of components in the fraction collector. As such, the combination of JP to be modified to add the operation device for adding chromatogram data as taught by Stevens, is said to meet the claims limitations and functional limitations, as the combined art recites all the given structural elements of the claims.

With regard to claims 1, 3-5, and 7 rejected under 35 USC 103(a) over JP in view of Windig (6,329,652), Applicant argues that the combination is improper. Applicant argues that Windig doe not expressly or implicitly indicate that spectrum intensities obtained in the plurality of spectrometry conditions are added to obtain chromatogram

data. Examiner asserts that Windig was provided for teaching of a method of data handling for an LC-MS system, and for adding particular data so as to obtain an enhanced chromatogram. As such, it would be obvious to modify JP as discussed, such that JP teaches an LC-MS system that may run in either positive or negative ion detection mode, thereby being the two particular datum to collect from in order to obtain an enhanced chromatogram.

With regards to claims 1, 3-5, and 7 rejected under 35 USC 103(a) over JP in view of Watanabe (6,444,979), Applicant argues that the combination is improper. Applicant argues that in Watanabe there is no express or implicit indication that spectrum intensities obtained in the plurality of spectrometry conditions are added to obtain chromatogram data. Examiner asserts that Watanabe was provided for the teaching of adding data in an chromatogram-MS system to obtain a chromatogram. Thereby, as JP teaches a similar system and a system that is operable under a plurality of ionization modes, it would be obvious to apply the adding of data taught by Watanabe to the multiple modes of the LC-MS system of JP.

With regards to claims 1, 3-5, and 7 rejected under 35 USC 103(a) over JP in view of Sacks (5,205,845), Applicant argues that the combination is improper. Applicant argues that the structure of Sacks includes multiple separation columns, compared to only one chromatograph portion in the present invention. Applicant further argues that since Sacks is provided with FID 16, it is widely known that a fraction collector is practically inapplicable to a gas chromatography with the FID, and thereby there is no motivation to combine the fraction collector and the FID. Examiner asserts that the

combination of JP and Sacks was not to add the FID as an additional structural element with the fraction collector, but that Sacks was relied upon for a teaching of adding data through multiple instances (multiple columns in Sacks, multiple modes in JP).

With regards to claims 1 and 3-7 rejected under 35 USC 103(a) over Bateman et al. (A Novel Precursor Ion Discovery Method on a Hybrid-Quadropole Orthoganol Acceleration Time-of-Flight (Q-TOF) Mass Spectrometer for Studying Protein Phosphorylation), hereafter Bateman, in view of Stevens (as well as over Windig; as well as over Watanabe; as well as over Sacks), Applicant argues that such a combination (as well as the others) is(are) improper.

Applicant argues that, as stated above, JP, Bateman, Stevens, Windig, Watanabe, and Sacks do not disclose that spectrum intensities obtained in the plurality of spectrometry conditions are added for each cycle of the mass spectrometry by a signal process portion to obtain chromatogram data. Examiner asserts that as discussed above, the specific functionalities of the fraction collector selective collecting in combination with the signal process portion has not received patentable weight as the control means, software, or other processing means with associated functions for such functionalities has not been recited in the claims at present. Further, Examiner asserts that, as discussed above and as with Stevens, there is taught a chromatogram system with two detector and a fraction collector, and the chromatogram data are added or subtracted to scale the data. Examiner thereby asserts that Bateman teaches a tandem system (applicable to the two detection system of Stevens), and it would thereby be obvious to add the data from the chromatograms generated by the fragmented and

unfragmented ionization detection of Bateman in order to scale the data in a similar two-detection scheme chromatograph such as taught by Stevens.

Examiner further asserts that, as discussed above, Applicant's recitation to the cycles of mass spectrometry with the control portion are indefinitely defined by the currently recited claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Neil Turk whose telephone number is 571-272-8914. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NT

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